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<b>(54) Title:</b> MULTI-PURPOSE CONTACT LENS CARE COMPOSITIONS  <b>(57) Abstract</b>  Multi-purpose solutions for contact lens care provide substantial lens wearer/user comfort and/or acceptability. Such solutions include an aqueous liquid medium; an antimicrobial component, preferably a biguanide polymer present in an amount of less than about 5 ppm; a surfactant component, preferably a poly(oxyethylene)-poly(oxypropylene) block copolymer surfactant, in an effective amount; a phosphate buffer component in an effective amount; a viscosity inducing component, preferably selected from cellulosic derivatives, in an effective amount; and a tonicity component in an effective amount. Such solutions have substantial performance, comfort and acceptability benefits, which, ultimately, lead to ocular health advantages and avoidance of problems caused by contact lens wear.		

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**MULTI-PURPOSE CONTACT LENS  
CARE COMPOSITIONS**

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**Background of the Invention**

The present invention relates to compositions for treating, for example, disinfecting, cleaning, soaking, conditioning and wetting contact lenses. More particularly, the invention relates to multi-purpose solutions useful in treating contact lenses, for example, for disinfecting contact lenses, for removing deposit material from contact lenses, for soaking, conditioning and/or wetting contact lenses and the like, which provide substantial comfort and acceptability benefits to the users of such solutions.

Contact lenses need to be periodically treated, for example, disinfected, cleaned, soaked and the like, on a regular basis because of the tendency for a variety of ocular and environmental contaminants, microbes and other materials to accumulate on the lenses and/or the need to provide the lenses in suitable condition for safe and comfortable wear. User compliance, that is users treating contact lenses on a regular and consistent basis, is important in order to promote ocular health and to avoid problems associated with contact lens wear. User compliance is enhanced when the treatment solution employed provides high degrees of lens wearer/user comfort and acceptability. Therefore, it would be advantageous to provide compositions for treating contact lenses which provide such comfort and/or are accepted by contact lens wearers/users of such compositions.

Fu U.S. Patent 4,323,467 discloses an aqueous composition combining a poly(oxyethylene)-poly(oxypropylene) substituted ethylenediamine surfactant, a germicidal agent, a viscosity builder, a tonicity agent, a sequestering agent and water for

treating rigid contact lenses. This patent discloses a germicide, such as thimerosal and/or benzalkonium chloride, in a concentration of 0.0005%-0.05%. The Fu patent does not disclose the use of any specific buffer.

5 Although the compositions of the Fu patent have multiple utilities, there is a potential for eye discomfort and/or irritation, for example, because of the relatively high concentrations of germicide and the apparent lack of pH control.

10 British Patent 1,432,345 discloses a contact lens disinfecting composition including an ophthalmically acceptable biguanide in a total amount of from 0.0005% to 0.05% by weight. This British patent discloses that the solution preferably has a pH of from 5 to 8 and  
15 employs a phosphate buffer. The patent also discloses employing additional bactericides, thickening agents and non-ionic surfactants, as well as disodium EDTA in concentrations of at least 0.1%. Although these compositions are effective as contact lens  
20 disinfectants, they do pose a risk of eye discomfort and/or irritation, for example, because of the relatively high concentrations of biguanide and EDTA employed.

Ogunbiyi et al U.S. Patent 4,758,595 discloses an  
25 aqueous solution of a biguanide in an amount of 0.000001 to 0.0003% weight percent in combination with a borate buffer system, EDTA, and one or more surfactants. This U.S. Patent additionally states that conventional buffers, other than the borate buffer, can be used but  
30 only in conjunction with increased amounts of biguanide. Thus, the general conclusion of this U.S. Patent is that if reduced amounts of biguanide are to be used, a borate buffer is essential. Although such compositions are useful, the potential for ocular discomfort and  
35 irritation in a relatively large percentage of the total

population still exists, for example, because of the requirement that a borate buffer be employed.

There continues to be a need to provide new contact lens treatment systems, for example, multi-purpose solutions, that effect the desired treatment or treatments of the lens and, at the same time, provide substantial, preferably enhanced, lens wearer/user comfort and acceptability.

10 Summary of the Invention

New compositions for treating contact lenses have been discovered. The present compositions, that is multi-purpose aqueous solutions, include antimicrobial components, preferably reduced concentrations of antimicrobial components, in combination with phosphate buffers and viscosity inducing components to provide the desired antimicrobial activity and performance effectiveness and, importantly, substantial, preferably enhanced, lens wearer/user comfort and acceptability benefits. These compositions are surprising and unexpected in view of the above-noted prior art which employs relatively large concentrations of antimicrobial components and/or buffering systems other than phosphate buffering systems and/or does not employ viscosity inducing components. In addition, the inclusion of one or more other components in the present compositions is effective in providing additional beneficial properties to the compositions, and preferably provide further lens wearer/user comfort and acceptability benefits. The present compositions have a multitude of applications, for example, as disinfecting, cleaning, soaking, wetting and conditioning compositions, for contact lens care, while providing substantial lens wearer/user comfort and acceptability. The present compositions preferably increase user compliance, that is promote regular and

consistent contact lens care, and, ultimately, lead to or facilitate better ocular health.

In one embodiment of the present invention, multi-purpose solutions for contact lens care are provided.

5 Such solutions comprise an aqueous liquid medium; an antimicrobial component in an amount effective to disinfect a contact lens contacted with the solution; a surfactant in an amount effective in cleaning a contact lens contacted with the solution; a phosphate buffer  
10 component in an amount effective in maintaining the pH of the solution within a physiologically acceptable range; a viscosity inducing component present in an effective amount; and a tonicity component in an amount effective in providing the desired tonicity to the  
15 solution.

The antimicrobial component may be any suitable, preferably ophthalmically acceptable, material effective to disinfect a contact lens contacted with the present solutions. Preferably, the antimicrobial component is  
20 selected from biguanides, biguanides polymers, salts thereof and mixtures thereof, and is present in an amount in the range of about 0.1 ppm to about 3 ppm or less than 5 ppm (w/v). The preferred relatively reduced concentration of the antimicrobial component has been  
25 found to be very effective, in the present compositions, in disinfecting contact lenses contacted with the compositions, while at the same time promoting lens wearer/user comfort and acceptability.

Any suitable, preferably ophthalmically acceptable,  
30 surfactant component which is effective in cleaning contact lenses may be employed. The surfactant component preferably is non-ionic and, more preferably, is selected from poly(oxyethylene)-poly(oxypropylene) block copolymers and mixtures thereof.

35 Any suitable, preferably ophthalmically acceptable, viscosity inducing or thickening agent may be included

in the present compositions. The viscosity inducing component preferably is selected from cellulosic derivatives and mixtures thereof and is present in an amount in the range of about 0.05% to about 0.5% (w/v).

5 Without wishing to limit the invention to any particular theory of operation, it is believed that the presence of a viscosity inducing component at least assists in providing the lens wearer/user comfort and acceptability benefits of the present invention, which  
10 promote regular and consistent contact lens care and ultimately lead to or facilitate better ocular health. The present combinations of components, for example, including such viscosity inducing components, are effective in providing the degree of lens wearer/user  
15 comfort and acceptability benefits described herein.

Although any suitable, preferably ophthalmically acceptable, tonicity component may be employed, a very useful tonicity component is a combination of sodium chloride and potassium chloride.

20 The present compositions preferably include an effective amount of a chelating component. Any suitable, preferably ophthalmically acceptable, chelating component may be included in the present compositions, although ethylenediaminetetraacetic acid  
25 (EDTA), salts thereof and mixtures thereof are particularly effective. More preferably, the present compositions include chelating components in effective amounts less than about 0.05% (w/v) and still more preferably 0.02% (w/v) or less. Such reduced amounts  
30 of chelating component in the present compositions remain effective in providing the desired chelating and/or sequestering functions while, at the same time, are better tolerated in the eye, thereby reducing the risk of user discomfort and/or ocular irritation.

35 Various combinations of two or more of the above-noted components may be used in providing at least one

of the benefits described herein. Therefore, each and every such combination is included within the scope of the present invention.

These and other aspects of the present invention  
5 are apparent in the following detailed description, examples and claims.

#### **Detailed Description of the Invention**

The present invention is directed to multi-purpose  
10 solutions useful for treating, for example, disinfecting, cleaning, soaking, rinsing, wetting, conditioning and the like, contact lenses. Any contact lenses, for example, conventional hard contact lenses, rigid gas permeable contact lenses and soft, hydrophilic  
15 or hydrogel, contact lenses, can be treated in accordance with the present invention.

In one embodiment, the present compositions comprise a liquid aqueous medium; an antimicrobial component in the liquid aqueous medium in an amount  
20 effective to disinfect a contact lens contacted with the composition; a surfactant, preferably a non-ionic surfactant, component in an amount effective in cleaning a contact lens contacted with the composition; a phosphate buffer component in an amount effective in  
25 maintaining the pH of the composition within a physiologically acceptable range; an effective amount of a viscosity inducing component; and an effective amount of a tonicity component. The present compositions preferably include an effective amount of a chelating or  
30 sequestering component, more preferably in a range of less than 0.05% (w/v). Each of the components, in the concentration employed, included in the solutions and the formulated solutions of the present invention preferably are ophthalmically acceptable. In addition,  
35 each of the components, in the concentration employed,

included in the present solutions preferably is soluble in the liquid aqueous medium.

A solution or component thereof is "ophthalmically acceptable" when it is compatible with ocular tissue, that is, it does not cause significant or undue detrimental effects when brought into contact with ocular tissue. Preferably, each component of the present compositions is also compatible with the other components of the present compositions. The present compositions are more preferably substantially ophthalmically optimized. An ophthalmically optimized composition is one which, within the constraints of component chemistry, minimizes ocular response, or conversely delivers ophthalmic benefit to the lens wearing eye.

The presently useful antimicrobial components include chemicals which derive their antimicrobial activity through a chemical or physiochemical interaction with microbes or microorganisms, such as those contaminating a contact lens. Suitable antimicrobial components are those generally employed in ophthalmic applications and include, but are not limited to, quaternary ammonium salts used in ophthalmic applications such as poly[dimethylimino-2-butene-1,4-diyl] chloride, alpha-[4-tris(2-hydroxyethyl) ammonium]-dichloride (chemical registry number 75345-27-6, available under the trademark Polyquaternium 17 from Onyx Corporation), benzalkonium halides, and biguanides, such as salts of alexidine, alexidine-free base, salts of chlorhexidine, hexamethylene biguanides and their polymers, and salts thereof, antimicrobial polypeptides, chlorine dioxide precursors, and the like and mixtures thereof. Generally, the hexamethylene biguanide polymers (PHMB), also referred to as polyaminopropyl biguanide (PAPB), have molecular weights of up to about 100,000. Such compounds are known and are disclosed in

Ogunbiyi et al U.S. Patent No. 4,758,595, the disclosure of which is hereby incorporated in its entirety by reference herein.

5 The antimicrobial components useful in the present invention preferably are present in the liquid aqueous medium in concentrations in the range of about 0.00001% to about 2% (w/v).

10 More preferably, the antimicrobial component is present in the liquid aqueous medium at an ophthalmically acceptable or safe concentration such that the user can remove the disinfected lens from the liquid aqueous medium and thereafter directly place the lens in the eye of safe and comfortable wear.

15 The antimicrobial components suitable for inclusion in the present invention include chlorine dioxide precursors. Specific examples of chlorine dioxide precursors include stabilized chlorine dioxide (SCD), metal chlorites, such as alkali metal and alkaline earth metal chlorites, and the like and mixtures thereof.

20 Technical grade sodium chlorite is a very useful chlorine dioxide precursor. Chlorine dioxide-containing complexes such as complexes of chlorine dioxide with carbonate, chlorine dioxide with bicarbonate and mixtures thereof are also included as chlorine dioxide

25 precursors. The exact chemical composition of many chlorine dioxide precursors, for example, SCD and the chlorine dioxide complexes, is not completely understood. The manufacture or production of certain chlorine dioxide precursors is described in McNicholas

30 U.S. Patent 3,278,447, which is incorporated in its entirety herein by reference. Specific examples of useful SCD products include that sold under the trademark Dura Klor by Rio Linda Chemical Company, Inc., and that sold under the trademark Anthium Dioxide by

35 International Dioxide, Inc.

If a chlorine dioxide precursor is included in the present compositions, it preferably is present in an effective contact lens disinfecting amount. Such effective disinfecting concentrations preferably are in the range of about 0.002 to about 0.06% (w/v) of the present compositions. Such chlorine dioxide precursors may be used in combination with other antimicrobial components, such as biguanides, biguanide polymers, salts thereof and mixtures thereof.

In the event that chlorine dioxide precursors are employed as antimicrobial components, the compositions preferably have an osmolality of at least about 200 mOsmol/kg and are buffered to maintain the pH within an acceptable physiological range, for example, a range of about 6 to about 10.

In one embodiment, the antimicrobial component is non-oxidative. It has been found that reduced amounts of non-oxidative antimicrobial components, for example, in a range of about 0.1 ppm to about 3 ppm or less than 5 ppm (w/v), in the present compositions are effective in disinfecting contact lenses and reduce the risk of such antimicrobial components causing ocular discomfort and/or irritation. Such reduced concentration of antimicrobial component is very useful when the antimicrobial component employed is selected from biguanides, biguanide polymers, salts thereof and mixtures thereof.

When a contact lens is desired to be disinfected by the present compositions, an amount of the antimicrobial component effective to disinfect the lens is used. Preferably, such an effective amount of the antimicrobial component reduces the microbial burden or load on the contact lens by one log order in three hours. More preferably, an effective amount of the disinfectant reduces the microbial load by one log order in one hour.

The phosphate buffer component is present in an amount effective to maintain the pH of the composition or solution in the desired range, for example, in a physiologically acceptable range of about 4 or about 5 or about 6 to about 8 or about 9 or about 10. In particular, the solution preferably has a pH in the range of about 6 to about 8. The phosphate buffer component preferably includes one or more phosphate buffers, for example, combinations of monobasic phosphates, dibasic phosphates and the like. Particularly useful phosphate buffers are those selected from phosphate salts of alkali and/or alkaline earth metals. Examples of suitable phosphate buffers include one or more of sodium dibasic phosphate ( $\text{Na}_2\text{HPO}_4$ ), sodium monobasic phosphate ( $\text{NaH}_2\text{PO}_4$ ) and potassium monobasic phosphate ( $\text{KH}_2\text{PO}_4$ ). The present buffer components frequently are used in amounts in a range of about 0.01% or about 0.02% to about 0.5% (w/v), calculated as phosphate ion.

The present compositions preferably further comprise effective amounts of one or more additional components, such as a detergent or surfactant component; a viscosity inducing or thickening component; a chelating or sequestering component; a tonicity component; and the like and mixtures thereof. The additional component or components may be selected from materials which are known to be useful in contact lens care compositions and are included in amounts effective to provide the desired effect or benefit. When an additional component is included, it is preferably compatible under typical use and storage conditions with the other components of the composition. For instance, the aforesaid additional component or components preferably are substantially stable in the presence of the antimicrobial and buffer components described herein.

A surfactant component preferably is present in an amount effective in cleaning, that is to at least facilitate removing, and preferably effective to remove, debris or deposit material from, a contact lens  
5 contacted with the surfactant-containing solution. Exemplary surfactant components include, but are not limited to, nonionic surfactants, for example, polysorbates (such as polysorbate 20-Trademark Tween 20), 4-(1, 1, 3, 3-tetramethylbutyl)  
10 phenol/poly(oxyethylene) polymers (such as the polymer sold under the trademark Tyloxapol), poly(oxyethylene)-poly(oxypropylene) block copolymers, glycolic esters of fatty acids and the like, and mixtures thereof.

The surfactant component preferably is nonionic,  
15 and more preferably is selected from poly(oxyethylene)-poly(oxypropylene) block copolymers and mixtures thereof. Such surfactant components can be obtained commercially from the BASF Corporation under the trademark Pluronic7. Such block copolymers can be  
20 generally described as polyoxyethylene/polyoxypropylene condensation polymers terminated in primary hydroxyl groups. They may be synthesized by first creating a hydrophobe of desired molecular weight by the controlled addition of propylene oxide to the two hydroxyl groups  
25 of propylene glycol. In the second step of the synthesis, ethylene oxide is added to sandwich this hydrophobe between hydrophile groups.

In accordance with a more preferred embodiment of the invention, such block copolymers having molecular  
30 weights in the range of about 2500 to 13,000 daltons are suitable, with a molecular weight range of about 6000 to about 12,000 daltons being still more preferred. Specific examples of surfactants which are satisfactory include: poloxamer 108, poloxamer 188, poloxamer 237,  
35 poloxamer 238, poloxamer 288 and poloxamer 407. Particularly good results are obtained poloxamer 237.

The amount of surfactant component, if any, present varies over a wide range depending on a number of factors, for example, the specific surfactant or surfactants being used, the other components in the composition and the like. Often the amount of surfactant is in the range of about 0.005% or about 0.01% to about 0.1% or about 0.5% or about 0.8% (w/v).

The viscosity inducing components employed in the present solutions preferably are effective at low or reduced concentrations, are compatible with the other components of the present solutions and are nonionic. Such viscosity inducing components are effective to enhance and/or prolong the cleaning and wetting activity of the surfactant component and/or condition the lens surface rendering it more hydrophilic (less lipophilic) and/or to act as a demulcent on the eye. Increasing the solution viscosity provides a film on the lens which may facilitate comfortable wearing of the treated contact lens. The viscosity inducing component may also act to cushion the impact on the eye surface during insertion and serves also to alleviate eye irritation.

Suitable viscosity inducing components include, but are not limited to, water soluble natural gums, cellulose-derived polymers and the like. Useful natural gums include guar gum, gum tragacanth and the like. Useful cellulose-derived viscosity inducing components include cellulose-derived polymers, such as hydroxypropyl cellulose, hydroxypropylmethyl cellulose, carboxymethyl cellulose, methyl cellulose, hydroxyethyl cellulose and the like. More preferably, the viscosity inducing agent is selected from cellulose derivatives (polymers) and mixtures thereof.

A very useful viscosity inducing component is hydroxypropylmethyl cellulose (HPMC).

The viscosity inducing component is used in an amount effective to increase the viscosity of the

solution, preferably to a viscosity in the range of about 1.5 to about 30, or even as high as about 750, cps at 25°C, preferably as determined by USP test method No. 911 (USP 23, 1995). To achieve this range of viscosity  
5 increase, an amount of viscosity inducing component of about 0.01% to about 5% (w/v) preferably is employed, with amounts of about 0.05% to about 0.5% being more preferred.

A chelating or sequestering component preferably is  
10 included in an amount effective to enhance the effectiveness of the antimicrobial component and/or to complex with metal ions to provide more effective cleaning of the contact lens.

A wide range of organic acids, amines or compounds  
15 which include an acid group and an amine function are capable of acting as chelating components in the present compositions. For example, nitrilotriacetic acid, diethylenetriaminepentacetic acid, hydroxyethylethylenediaminetriacetic acid, 1,2-diaminocyclohexane  
20 tetraacetic acid, hydroxyethylaminodiacetic acid, ethylenediamine-tetraacetic acid and its salts, polyphosphates, citric acid and its salts, tartaric acid and its salts, and the like and mixtures thereof, are useful as chelating components.  
25 Ethylenediaminetetraacetic acid (EDTA) and its alkali metal salts, are preferred, with disodium salt of EDTA, also known as disodium edetate, being particularly preferred.

The chelating component preferably is present in an  
30 effective amount, for example, in a range of about 0.01% and about 1% (w/v) of the solution.

In a very useful embodiment, particularly when the chelating component is EDTA, salts thereof and mixtures thereof, a reduced amount is employed, for example, in  
35 the range of less than about 0.05% (w/v) or even about 0.02% (w/v) or less. Such reduced amounts of chelating

component have been found to be effective in the present compositions while, at the same time, providing for reduced discomfort and/or ocular irritation.

The liquid aqueous medium used is selected to have  
5 no substantial deleterious effect on the lens being treated, or on the wearer of the treated lens. The liquid medium is constituted to permit, and even facilitate, the lens treatment or treatments by the present compositions. The liquid aqueous medium  
10 advantageously has an osmolality in the range of at least about 200 mOsmol/kg for example, about 300 or about 350 to about 400 mOsmol/kg. The liquid aqueous medium more preferably is substantially isotonic or hypertonic (for example, slightly hypertonic) and/or is  
15 ophthalmically acceptable.

The liquid aqueous medium preferably includes an effective amount of a tonicity component to provide the liquid medium with the desired tonicity. Such tonicity components may be present in the liquid aqueous medium  
20 and/or may be introduced into the liquid aqueous medium. Among the suitable tonicity adjusting components that may be employed are those conventionally used in contact lens care products, such as various inorganic salts. Sodium chloride and/or potassium chloride and the like  
25 are very useful tonicity components. The amount of tonicity component included is effective to provide the desired degree of tonicity to the solution. Such amount may, for example, be in the range of about 0.4% to about 1.5% (w/v). If a combination of sodium chloride and  
30 potassium chloride is employed, it is preferred that the weight ratio of sodium chloride to potassium chloride be in the range of about 3 to about 6 or about 8.

Methods for treating a contact lens using the herein described compositions are included within the  
35 scope of the invention. Such methods comprise contacting a contact lens with such a composition at

conditions effective to provide the desired treatment to the contact lens.

The contacting temperature is preferred to be in the range of about 0°C to about 100°C, and more preferably in the range of about 10°C to about 60°C and still more preferably in the range of about 15°C to about 30°C. Contacting at or about ambient temperature is very convenient and useful. The contacting preferably occurs at or about atmospheric pressure. The contacting preferably occurs for a time in the range of about 5 minutes or about 1 hour to about 12 hours or more.

The contact lens can be contacted with the liquid aqueous medium by immersing the lens in the medium. During at least a portion of the contacting, the liquid medium containing the contact lens can be agitated, for example, by shaking the container containing the liquid aqueous medium and contact lens, to at least facilitate removal of deposit material from the lens. After such contacting step, the contact lens may be manually rubbed to remove further deposit material from the lens. The cleaning method can also include rinsing the lens substantially free of the liquid aqueous medium prior to returning the lens to a wearer's eye.

The following non-limiting examples illustrate certain aspects of the present invention.

#### EXAMPLE 1

A solution is prepared by blending together the following components:

	PHMB (polyhexamethylene biguanide)	1 ppm (w/v)
35	Disodium EDTA	0.02% (w/v)
	Poloxamer 237 (poly(oxyethylene)-poly (oxypropylene) block	0.05% (w/v)

	copolymer)	
5	Sodium Phosphate Dibasic (heptahydrate)	0.12% (w/v)
	Sodium Phosphate Monobasic (monohydrate)	0.01% (w/v)
10	HPMC (Hydroxypropylmethyl Cellulose)	0.15% (w/v)
	Sodium Chloride	0.79% (w/v)
15	Potassium Chloride	0.14% (w/v)
	Water (USP)	Q.S. 100%

Approximately three (3) ml of this solution is introduced into a lens vial containing a lipid, oily deposit laden, hydrophilic or soft contact lens. The contact lens is maintained in this solution at room temperature for at least about four (4) hours. This treatment is effective to disinfect the contact lens. In addition, it is found that a substantial portion of the deposits previously present on the lens has been removed. This demonstrates that this solution has substantial passive contact lens cleaning ability. Passive cleaning refers to the cleaning which occurs during soaking of a contact lens, without mechanical or enzymatic enhancement.

After this time, the lens is removed from the solution and is placed in the lens wearer's eye for safe and comfortable wear. Alternately, after the lens is removed from the solution, it is rinsed with another quantity of this solution and the rinsed lens is then placed in the lens wearer's eye for safe and comfortable wear.

EXAMPLE 2

Example 1 is repeated except that the lens is rubbed and rinsed with a different quantity of the solution prior to being placed in the lens vial. After at least about four (4) hours, the lens is removed from the solution. The lens is then placed in the lens wearer's eye for safe and comfortable wear.

10

EXAMPLE 3

The solution of Example 1 is used as a long-term soaking medium for a hydrophilic contact lens. Thus, approximately three (3) ml of this solution is placed in a vial and a contact lens is maintained in the solution at room temperature for about sixty (60) hours. After this soaking period, the lens is removed from the solution and placed in the lens wearer's eye for safe and comfortable wear. Alternately, after the lens is removed from the solution, it is rinsed with another quantity of this solution and the rinsed lens is then placed in the lens wearer's eye for safe and comfortable wear.

25

EXAMPLE 4

A hydrophilic contact lens is ready for wear. In order to facilitate such wearing, one or two drops of the solution of Example 1 is placed on the lens immediately prior to placing the lens in the lens wearer's eye. The wearing of this lens is comfortable and safe.

35

**EXAMPLE 5**

A lens wearer wearing a contact lens applies one or two drops of the solution of Example 1 in the eye wearing the lens. This effects a re-wetting of the lens and provides for comfortable and safe lens wear.

**EXAMPLE 6**

A series of tests are conducted to evaluate the comfort, safety and acceptability of the solution prepared in accordance with Example 1 compared to two other solutions.

The first of these other solutions, referred to hereinafter as Composition A, is sold under the trademark ReNu7 by Bausch & Lomb and includes 0.5 ppm PHMB, a poly(oxyethylene)-poly(oxypropylene) substituted ethylenediamine surfactant, a borate buffer system, 0.1% disodium EDTA, and sodium chloride as a tonicity agent.

The second of these other solutions, referred to hereinafter as Composition B, is similar to the composition of Example 1 except that Composition B included 0.6% (w/v) tromethamine, and neither of the phosphates.

Each of these compositions is tested to evaluate its comfort, safety and acceptability for the care of hydrogel (hydrophilic) contact lenses worn on a daily basis among subjects previously adapted to at least one commercially available multi-purpose solution.

The study is a randomized, double-masked, three-way cross over study. The study is broken down into a series of three (3) one (1) month treatment periods. Each of the compositions is used on a daily basis for cleaning, rinsing after cleaning, disinfection, and rinsing prior to lens application, as needed. Because

each treatment period is only one (1) month in duration, no enzymatic cleaner is used in this study.

The subjects are evaluated at day zero (baseline), day seven (7) and day thirty (30) for each of the three  
 5 (3) treatment periods. The primary comfort and acceptability variables are lens wearing comfort and end of study product preference. The primary safety variable is slit lamp examination findings.

123 subjects are enrolled. 116 (94.3%) complete  
 10 Preference Questionnaires for Treatment Period 2. 118 (95.9%) complete Preference Questionnaires for Treatment Period 3.

The results of this study are summarized as follows. The slit lamp examinations indicate that each  
 15 of the compositions tested is acceptably safe. The comfort and acceptability results included in this summary are based on subjective answers to selected questions (at the end of Treatment Periods 2 and 3).

Further tabulations are made based on subjective  
 20 answers to the selected questions noted above, as well as to other questions included in the Preference Questionnaires. These tabulations are made using answers from the Preference Questionnaires for Treatment Period 3.

25 Results of these further tabulations are as follows:

Preference Question	Respondents Preferring		Respondents Preferring		No Preference	P Value
	Example 1 Composition	%	Composition A	%		
Overall preference	65		28		7	0.02
In-the-hand preference	56		27		17	0.02
In-the-eye preference	63		27		11	0.02
Comfort in-the-eye	60		25		15	0.02
Amount of time for lenses to settle in the eye	47		21		32	0.02
Keeping lenses moist in eyes	55		28		17	0.02
Keeping lenses lubricated in eyes	57		28	15		0.02
Soothing in eyes	57		27	16		0.02

\* BASED ON A P-VALUE OF 0.02, THESE RESULTS ARE SIGNIFICANT AT A 95% LEVEL OF CONFIDENCE

	<u>Preference Question</u>	<u>Respondents</u>		<u>No Preference</u>	<u>P Value</u>
		<u>Preferring Composition B Composition</u>	<u>Preferring Composition A</u>		
5		%	%		
	Overall preference	55	40	5	0.18
	In-the-hand preference	51	31	18	0.08
	In-the-eye preference	60	34	6	0.02
10	Comfort in-the-eye	36	34	10	0.06
	Amount of time for lenses to settle in the eye	44	31	25	0.26
	Keeping lenses moist in eyes	47	34	19	0.26
15	Keeping lenses lubricated in eyes	47	32	21	0.18
	Soothing in eyes	57	32	10	0.02

20           These results indicate a clear preference of the composition of Example 1 over Composition A; and an overall preference of the composition of Example 1 over Composition B.

          These results are indeed surprising since  
25   Composition A is a commercially available multi-purpose solution. Possible reasons for the preference of the Example 1 composition relative to Composition A include one or more of the presence of HPMC, the presence of a poly(oxyethylene)-poly(oxypropylene) block copolymer  
30   surfactant, the presence of the phosphate buffer, and/or the presence of a reduced amount of EDTA.

#### EXAMPLE 7

35           A solution containing 1 ppm (0.0001% (w/v)) polyhexamethylene biguanide (PHMB), 0.02% (w/v) EDTA, 0.05% (w/v) polyoxamer 237, 0.15% (w/v) hydroxypropylmethyl cellulose (HPMC), 0.12% (w/v) sodium phosphate dibasic, 0.01% (w/v) sodium phosphate  
40   monobasic, 0.79% (w/v) sodium chloride and 0.14% (w/v) potassium chloride was distributed into a set of tubes, 8 ml per tube. Each tube was given an initial inoculation of one of the organisms listed in the Table below. The tubes were permitted to incubate for 24  
45   hours at 32° C, with aliquots taken from each tube at 1, 2, 3, 4, and 24 hours. A negative control contained a solution of physiological saline solution inoculated

with each test organism. In each aliquot the PHMB was neutralized by adding 1 ml of the test solution to 9 ml of Letheen Broth. Letheen Broth contains lecithin and TWEEN® 80, a non-ionic surfactant; these ingredients  
 5 form micelles around the PHMB rendering it inactive without having a deleterious effect on the test bacteria and fungi. Serial dilutions of the neutralized aliquot were made and the dilutions plated onto Petri dishes containing either Tryptic Soy agar (bacteria) or  
 10 Sabouraud Dextrose agar (fungi). The plates were permitted to incubate for 48 hours, then the number of colonies counted.

The number of viable cells in each aliquot after incubation with the test solution was determined by  
 15 multiplying the number of colonies obtained on the culture plates by the dilution factor. Comparison of the number of colonies (viable cells) in each tube and time point with the negative control yielded the data contained in the Table below.

20

	<i>Serratia marcescens</i>		<i>Staphylococcus aureus</i>		<i>Pseudomonas aeruginosa</i>		<i>Fusarium solani</i>	
	Cfu/ml	Log Drop	Cfu/ml	Log Drop	Cfu/ml	Log Drop	Cfu/ml	Log Drop
Initial Inoculum	$7.0 \times 10^8$	NA	$7.0 \times 10^8$	NA	$5.0 \times 10^8$	NA	$4.0 \times 10^8$	NA
1 hour	$1.0 \times 10^3$	3.7	$2.0 \times 10^3$	2.5	<10	>4.4	$2.0 \times 10^8$	1.3
2 hours	40	4.2	$6.0 \times 10^2$	3.1	<10	>4.4	$2.0 \times 10^8$	1.3
3 hours	<10	>5.2	$7.0 \times 10^2$	3.0	<10	>4.4	$2.0 \times 10^8$	1.3
4 hours	<10	>5.2	$7.0 \times 10^1$	4.0	<10	>4.4	$2.0 \times 10^8$	1.3
24 hours							$9.0 \times 10^2$	2.5

As the data demonstrate, substantial microbiocidal activity is provided by the solutions of the present invention.

25 The present compositions provide a very beneficial and advantageous combination of performance efficacy and lens wearer/user comfort and acceptability. In the context of contact lens care solutions, lens wearer/user

comfort and acceptability are very important, for example, to promote regular and effective treating of contact lenses. Such treating of contact lenses ultimately promotes ocular health and reduces the frequency of problems caused by wearing contact lenses.

Thus, lens wearer/user comfort and acceptability are of substantial importance and benefit in a contact lens care product, in particular in the present compositions which exhibit substantial, even enhanced, lens wearer/user comfort and acceptability.

While this invention has been described with respect to various specific examples and embodiments, it is to be understood that the invention is not limited thereto and that it can be variously practiced within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A multi-purpose solution for contact lens care comprising:
  - 5 an aqueous liquid medium;  
an antimicrobial component in an amount effective to disinfect a contact lens contacted with said solution, said non-oxidative antimicrobial component being selected from the group consisting of  
10 biguanides, biguanide polymers, salts thereof and mixtures thereof, and being present in an amount in a range of about 0.1 ppm to about 3 ppm;  
a poly(oxyethylene)-poly(oxypropylene) block copolymer surfactant in an amount effective in cleaning  
15 a contact lens contacted with said solution;  
a phosphate buffer component in an amount effective in maintaining the pH of said solution within a physiologically acceptable range;  
a viscosity inducing component selected from  
20 the group consisting of cellulosic derivatives and mixtures thereof in an effective amount in a range of about 0.05% to about 0.5% (w/v);  
a chelating component in an effective amount of less than 0.05%(w/v); and  
25 a tonicity component in an amount effective in providing the desired tonicity to said solution.
2. The multi-purpose solution of claim 1 wherein said antimicrobial component is selected from the group  
30 consisting of polyhexamethylene biguanide, salts thereof and mixtures thereof.
3. The multi-purpose solution of claim 1 wherein said surfactant is present in an amount in the range of  
35 about 0.01% to about 0.8%(w/v).

4. The multi-purpose solution of claim 1 wherein said phosphate buffer component includes a combination of sodium hydrogen phosphate and sodium dihydrogen phosphate.

5

5. The multi-purpose solution of claim 1 wherein said phosphate buffer component is present in an amount in a range of about 0.01% to about 0.5%(w/v).

10

6. The multi-purpose solution of claim 1 wherein said viscosity inducing component is hydroxypropylmethyl cellulose.

7. The multi-purpose solution of claim 1 wherein  
15 said tonicity component includes a combination of sodium chloride and potassium chloride and is present in a range of about 0.4% to about 1.5%(w/v).

8. The multi-purpose solution of claim 1 wherein  
20 said chelating component is EDTA.

9. A multi-purpose solution for contact lens care comprising:

an aqueous liquid medium;

25

an antimicrobial component selected from the group consisting of biguanides, biguanide polymers, salts thereof and mixtures thereof, and being present in an amount in a range of about 0.1 ppm to less than 5 ppm;

30

a surfactant component in an amount effective in cleaning a contact lens contacted with said solution;  
a phosphate buffer component in an amount effective in maintaining the pH of said solution within a physiologically acceptable range;

a viscosity inducing component in an amount effective in increasing the viscosity of said solution; and

5 a tonicity component in an amount effective in providing the desired tonicity to said solution.

10 10. The multi-purpose solution of claim 9 wherein said antimicrobial component is selected from the group consisting of polyhexamethylene biguanide, salts thereof and mixtures thereof.

15 11. The multi-purpose solution of claim 9 wherein said viscosity inducing component is hydroxypropylmethyl cellulose.

20 12. The multi-purpose solution of claim 9 wherein said surfactant is selected from the group consisting of poly(oxyethylene)-poly(oxypropylene) block copolymers and mixtures thereof, and is present in an amount in a range of about 0.01% to about 0.8%(w/v).

25 13. The multi-purpose solution of claim 9 wherein said tonicity component includes a combination of sodium chloride and potassium chloride and is present in a range of about 0.4% to about 1.5%(w/v).

30 14. The multi-purpose solution of claim 9 which further comprises an effective amount of EDTA in a range of less than 0.05%(w/v).

15. A multi-purpose solution for contact lens care comprising:

35 an aqueous liquid medium;  
an antimicrobial component in an amount effective to disinfect a contact lens contacted with said solution;

a surfactant component in an amount effective in cleaning a contact lens contacted with said solution;

a phosphate buffer component in an amount effective in maintaining the pH of said solution within  
5 a physiologically acceptable range;

a viscosity inducing component selected from the group consisting of cellulosic derivatives and mixtures thereof and being present in an effective amount in a range of about 0.05% to about 0.5%(w/v);

10 a chelating component in an effective amount of less than 0.05%(w/v); and

a tonicity component in an amount effective in providing the desired tonicity to said solution.

15 16. The multi-purpose solution of claim 15 wherein said viscosity inducing component is hydroxypropylmethyl cellulose.

20 17. The multi-purpose solution of claim 15 wherein said chelating agent is EDTA.

18. The multi-purpose solution of claim 15 wherein said antimicrobial component is selected from the group consisting of biguanides, biguanide polymers, salts  
25 thereof and mixtures thereof, and is present in an amount in a range of about 0.1 ppm to less than 5 ppm.

19. The multi-purpose solution of claim 18 wherein said antimicrobial component is selected from the group consisting of polyhexamethylene biguanide, salts thereof  
30 and mixtures thereof.

20. The multi-purpose solution of claim 15 wherein said surfactant is present in an amount in a range of  
35 about 0.01% to about 0.8%(w/v).

# INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 98/25378

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61L2/18

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 758 595 A (OGUNBIYI LAI ET AL) 19 July 1988 cited in the application see column 3, line 27 - line 32 see column 4, line 57 - column 5, line 4 ---	1-20
X	WO 94 15649 A (POLYMER TECHNOLOGY CORP) 21 July 1994 see page 4, paragraph 2 - paragraph 3 see page 5, paragraph 3 - page 7, paragraph 2 see table 1 ---	1-20
A	GB 1 432 345 A (SMITH ENPHEW RESEARCH LTD) 14 April 1976 see page 2, line 32 - page 3, line 17 see example 1 -----	1-20



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Information on patent family members

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